

U.S.S.N. 10/623,383

Filed: July 18, 2003

AMENDMENT AND RESPONSE TO RESTRICTION REQUIREMENT

Amendment

In the Claims

Please amend the claims as follows:

1. (currently amended) A method of using a glycosaminoglycan-degrading enzyme to treat, remove and degrade glycosaminoglycans from proteoglycans comprising administering to an individual in need of treatment an effective amount of a glycosaminoglycan-degrading enzyme to ~~inhibit endothelial cell proliferation~~ treat a cell proliferation disorder selected from the group consisting of rheumatoid arthritis, psoriasis, ocular angiogenic diseases, rubeosis, Osler-Webber Syndrome, myocardial angiogenesis, plaque neovascularization, telangiectasia, hemophiliac joints, angiofibroma, disease of excessive or abnormal stimulation of endothelial cells, Crohn's disease, atherosclerosis, scleroderma, and hypertrophic scars, diseases that have angiogenesis as a pathologic consequence, adhesions, scarring, cirrhosis of the liver, pulmonary fibrosis following acute respiratory distress syndrome or other pulmonary fibrosis of the newborn, endometriosis, polyposis, obesity, uterine fibroids, prostatic hypertrophy, and amyloidosis.

2. (currently amended) The method of claim 1 wherein the enzyme is a selected from the group consisting of bacterial glycosaminoglycan degrading enzyme ~~is selected from the group consisting of~~ heparinase 1 from *Flavobacterium heparinum*, heparinase 2 from *Flavobacterium heparinum*, heparinase 3 from *Flavobacterium heparinum*, chondroitinase AC from *Flavobacterium heparinum*, and chondroitinase B from *Flavobacterium heparinum*, heparinase from *Bacteroides* strains, heparinase from *Flavobacterium* Hp206, heparinase from *Cytophagia* species, chondroitin sulfate degrading enzymes from *Bacteroides* species, chondroitin sulfate degrading enzymes from *Proteus vulgaris*, chondroitin sulfate degrading

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enzymes from *Microcossus*, chondroitin sulfate degrading enzymes from *Vibrio* species, chondroitin sulfate degrading enzymes from *Arthrobacter aureus*, these enzymes expressed from recombinant nucleotide sequences in bacteria and combinations thereof.

3. (cancelled)

4. (Original) The method of claim 1 wherein the enzyme is a chondroitinase.

5. (currently amended) The method of claim 4 wherein the chondroitinase is selected from the group consisting of chondroitinase AC, chondroitinase B and a combination thereof thereof.

6. (previously presented) The method of claim 1 wherein the individual has a disorder involving cell proliferation.

7. (previously presented) The method of claim 6 wherein the enzyme is chondroitinase AC.

8. (currently amended) The method of claim 1 wherein the individual has a disorder ~~is in which cell proliferation is involved, the disorder being selected from the group consisting of~~ ~~rheumatoid arthritis; psoriasis; ocular angiogenic diseases; rubeosis; Osler-Webber Syndrome;~~ ~~myocardial angiogenesis; plaque neovascularization; telangiectasia; hemophilic joints;~~ ~~angiofibroma; disease of excessive or abnormal stimulation of endothelial cells; Crohn's disease;~~ ~~atherosclerosis, scleroderma, and hypertrophic scars, diseases that have angiogenesis as a~~ ~~pathologic consequence, adhesions, scarring, cirrhosis of the liver, pulmonary fibrosis following~~ ~~acute respiratory distress syndrome or other pulmonary fibrosis of the newborn, endometriosis,~~ ~~polypoid, obesity, uterine fibroids, prostatic hypertrophy, and amyloidosis.~~

9. (Original) The method of claim 1 wherein the enzyme is administered systemically.

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10. (Original) The method of claim 1 wherein the enzyme is administered topically or locally at or adjacent a site in need of treatment.

11. (Original) The method of claim 1 wherein the enzyme is administered in a controlled and/or sustained release formulation.

12. (previously presented) A formulation for administration to an individual in need of treatment thereof for a disorder involving cell proliferation, the formulation comprising an effective amount of a glycosaminoglycan degrading enzyme to inhibit endothelial cell proliferation, wherein the dosage is different than the amount effective for enhancing wound healing, and

a pharmaceutically acceptable carrier.

13. (Original) The formulation of claim 12 wherein the enzyme is selected from the group consisting of bacterial glycosaminoglycan degrading enzyme is selected from the group consisting of heparinase 1 from *Flavobacterium heparinum*, heparinase 2 from *Flavobacterium heparinum*, heparinase 3 from *Flavobacterium heparinum*, chondroitinase AC from *Flavobacterium heparinum*, and chondroitinase B from *Flavobacterium heparinum*, heparinase from *Bacteroides* strains, heparinase from *Flavobacterium* Hp206, heparinase from *Cytophagia* species, chondroitin sulfate degrading enzymes from *Bacteroides* species, chondroitin sulfate degrading enzymes from *Proteus vulgaris*, chondroitin sulfate degrading enzymes from *Micrococcus*, chondroitin sulfate degrading enzymes from *Vibrio* species, chondroitin sulfate degrading enzymes from *Arthrobacter aurescens*, these enzymes expressed from recombinant nucleotide sequences in bacteria and combinations thereof.

14. (cancelled)

15. (Original) The formulation of claim 12 wherein the enzyme is a chondroitinase.

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16. (Original) The formulation of claim 15 wherein the chondroitinase is chondroitinase AC.

17. (Original) The formulation of claim 12 wherein the enzyme is in a controlled, sustained release formulation.

18. (previously presented) The formulation of claim 12 wherein the enzyme is formulated in combination with a compound selected from the group consisting of antibiotics, cytokines and anti-inflammatories.